Management of PEDIATRIC ASTHMA - Made Easy !

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Pediatric Asthma

Why It is a very important topic ?

هتقدروا مدى أهميته ، طا تتعرفوا على بعض الحقائق المرعبة 👀

Regarding the epidemiology :

- It is the most common chronic disease of childhood
- Prevalence (10 - 15 %)

نقول أرقاماً ...
وفي بعض الدول أعلى من كده ...
يعني مثلاً في أستراليا ١٨٪ في السعودية ٢٥٪ في أوروجواي والبرازيل ٣٠٪.
٣٠٠ مليون على مستوى العالم

one child
hospitalized with asthma attack
every 8 minutes

Regarding the diagnosis :

الفقرة الأولى
- It is astonishing that, in 21st century there is no test your child can take to tell if he is definitely asthmatic or not !

الفقرة الثانية
- Doctors are overdiagnosing asthma in children !

"دراسة في أستراليا"
100 children with chronic cough investigated
- before investigation: 50 % were diagnosed as asthma
- after investigation: only 5 % were really asthmatic

"دراسة في هولندا"
half of all children asthma cases are overdiagnosed

Regarding Treatment :

- Despite overdiagnosis, most children with asthma are inappropriately treated !

- Underprescription of controller medications
- overprescription of relievers medications

لا أحد منزه عن كل ذلك
أدى هذه الأخطاء المتجذرة في التشخيص والعلاج بتجعل
على الرغم من وجود
Multiple Guidelines

- GINA (Global Initiative for Asthma) since 1993 ← WHO
- NICE + BTS / SIGN (في إنجلترا) ← National Lung, Heart & Blood institute USA
- Australian
- Japanese
- Chinese
- SINA (Saudi Initiative for Asthma)

واضح إنه كل هذا الكم
عمل
confusion & uncertainty
for
clinicians

Management of Pediatric Asthma

Management vs **Treatment**

Management ↓ كلمة أكثر شمولية

Treatment ↓ (علاج المرض)

= The overall strategy, including :

1- Treatment (وما قبله / ومابعده)

2- Pre- & Post- Treatment aspects

- Pre- → Diagnosis
- Post- → Prognosis & Follow-up

(بالنسبة للنطق)
(UK) ← أسما
(US) ← أزما

Origin of the word "Asthma"

* هي كلمة (يونانية الأصل) معناها الحرفي :
to exhale with open mouth = panting (لهاث)
وكان الطبيب اليوناني الأشهر الملقب بأبو الطب (أبقراط) هو أول من أطلقها ... "حوالي ٤٠٠ سنة قبل الميلاد"
to describe any patient with breathlessness / dyspnea
(due to any cardiopulmonary problem) !

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* ظلت القصة على هذا المنوال حتى أوائل القرن الـ ١٩ :
when it was recognized as a unique airway disorder characterized by bronchospasm !
(Rene Laennec) وكان ذلك على يد الطبيب الفرنسي الشهير
مخترع السماعة

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* The concept of Allergic nature of asthma
كانت في أواخر القرن الـ ١٩
The concept of Inflammatory nature of asthma
كانت في أوائل القرن الـ ٢٠
The role of Ig-E in mast cell activation
سنة ١٩٦٦م
The concept of predominance of TH_2 cells & its released Cytokine profile
سنة ١٩٩٠م

والشغل الآن في القرن الحادي والعشرين على الـ
Genetic analysis of atopic persons
(more than 200 genetic risk factors identified to explain development of atopic diseases : Asthma / ARIAD) !
(genome analysis of 360.000 children by international team
أساتذة جامعات من أمريكا وأوروبا وأستراليا)

Diagnostic Pathway of Asthma

"Children with respiratory symptoms of asthma"

↓

Take a structured **clinical history**, specifically check for:

- Cough, wheeze, dyspnea – any daily or seasonal variation of these symptoms
- any triggers that make symptoms worse → exercise, smoking, pets, cold air, excitement
- personal or family history of atopy

N.B.

Don't use symptoms alone without an objective test to diagnose asthma
Don't use history of atopy alone to diagnose asthma

↓

Examine children with suspected asthma to identify:

- expiratory polyphonic wheeze
- signs of other causes of respiratory symptoms

N.B.

Even if examination results are normal, the child may still have asthma

- Perform spirometry for children with symptoms suggestive of asthma
- Consider BDR-test if spirometry shows an obstruction

unable to do
(young children < 5 y)

Treat symptoms based on clinical judgement ...
& Review the child on regular basis
هنرجعلها تاني في الآخر

-ve

FeNO test
Peak Flow Variability test

لازم نعمل الاتنين مع بعض

+ve

Diagnose Asthma
(أو يلي الخمس)

Both are -ve

Consider Alternative Diagnosis & Refer for Specialist assessment

One is +ve

Suspect Asthma
& Review diagnosis after treatment

Both are +ve

Diagnose Asthma
(أو يلي الخمس)

« Diagnostic Summary »

Clinical Assessment

Objective Testing

	Test	Threshold level
	Obstructive Spirometry	$FEV_1 / FVC < 70\%$
15 minutes after SABA inhalation	Bronchodilatory Reversibility (BDR)	$FEV_1 \uparrow \geq 12\%$
	$FeNO$	≥ 35 ppb
monitored for 2 – 4 weeks	Peak Flow Variability	$> 20\%$

N.B.

Don't offer the following as diagnostic tests for asthma :

1- skin prick tests to aeroallergens
2- serum total & specific Ig-E
3- peripheral blood esinophilia

Use serum prick tests or serum specific Ig-E tests to identify triggers after diagnosis of asthma has been made

No single Reliable Test for diagnosis of asthma

Reliability

"assessed by"

Accuracy
(sensitivity & specificity)

Reproducibility
(when repeated on the same sample → gives the same result)

FeNO

* It may not detect asthma in a patient with chest infection or in a patient who smokes
(false -ve results)

also in:
- cardiac disease
- GERD
- cystic fibrosis
- PCD ciliary dyskinesia

Spirometry

* Majority of patients with asthma will have normal spirometry (70%)
وبالتالي
(high false -ve results)

So,

normal spirometry does not exclude asthma

Marker of:
esinophilic, Th2-mediated airway inflammation !!

يثبت أن

FeNO Test
(Fractional exhaled Nitric Oxide)

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* Advantages :
- × Non-invasive
- × Portable (وزنه ٤٠٠ جم)
- × Easy to use
- × Quick (10 seconds)
- × Quantitative

الجهاز ثمنه ١٨٠٠ يورو
شركة : فيلبس
لها موزعين في :
السعودية / الإمارات / الكويت / البحرين
لبنان / الجزائر / المغرب ...
والغريب عدم وجود موزعين في مصر
!!

* Diagnostic utility :
- × Confirm diagnosis of asthma, especially in young children !
  (high levels indicate ongoing allergic inflammation in the airway)
- × Determine corticosteroid responsiveness & adherence

NICE 2017
advocates a central role for FeNO test
in diagnosis of asthma

* Cut-off values :
- × Low
  = < 20 ppb (parts per billion)
- × High
  = > 35 ppb (in children)
  = > 50 ppb (in adults)

نسبة بين الأطفال الأقل من ٥ سنوات

About 50% of children are reported to have wheezing in the first year of life ...
Parents of these children often ask:
Does my child have asthma?

"3 Phenotypes of wheezy children"

60%	20%	20%
Transient Early Wheezers	Non-Atopic Wheezers	Ig-E mediated or Atopic Wheezers
✓	✓	✓
• resolve before school age	• resolve by age 10	• continue to wheeze during adolescence
risk factors are: prematurity & maternal smoking		

modified API
(Asthma Predictive Index)

* **Applied to :**

children below 3y with ≥ 4 documented wheezing episodes in the past year .

* **Positive when :**

One or more **Major** Criteria
1- Parent with asthma
2- Patient with atopic eczema
3- +ve skin or blood test for aeroallergen

Or

Two or more **Minor** Criteria
1- Wheezing unrelated to cold
2- esinophilia ≥ 4 %
3- Food allergy to milk, egg, or peanut
(most prevalent allergens)
في الأطفال

* **Clinical significance :**

Wheezy child with +ve API
= 80 % chance that child would have a definite diagnosis of asthma when entering first grade !

Long-Term Goals of Asthma Management

Symptom Control

to
maintain
normal
activity level

Risk Reduction

=
minimize risk factors
for
poor future outcome

اللي هو ريه ؟

1- exacerbations
2- fixed airflow limitation
3- medication side-effects

C_1 : How to assess level of symptom control ?

؟ (٤) أسئلة عن حالة المريض في آخر (٤) أسابيع

item	Well Controlled	Partly Controlled	Un Controlled
(1) Daily symptoms (⩾ 2 / last week) Yes / No	Score 0		
(2) Nocturnal symptoms (⩾ 2 / last month) Yes / No !! تعكيه عن النوم ليلاً		Score 1 – 2	
(3) Use of reliever (⩾ 2 / last week) Yes / No			Score 3 – 4
(4) Any activity limitation Yes / No			

C_2 : What are the risk factors for exacerbations ?

1- Uncontrolled symptoms
2- ⩾ 1 severe exacerbation / last year (استدعت دخوله المستشفى)
3- Smoking
4- Obesity
5- Allergen exposure
6- Confirmed food allergy
7- Psychological problems
8- Socio-economic problems
9- Low FEV1 esp. if below 60% (if applicable)
10- Sputum esinophilia (in limited centres)

Classification of Asthma Medications

3 Categories

Reliever (Rescue) Medications

- taken as-needed to relieve symptoms
- = SABA (short-acting β_2 agonists)

All Patients

Controller (Preventer) Medications

- taken on regular daily basis to ↓ airway inflammation & ↓ risk of exacerbation
- = ICS (inhaled corticosteroids)

Most Patients

Add-on Therapies
دوائية / غير دوائية

- علاج إضافي مينفعش ياخد لوحده لازم يضاف إلى الـ "standard controller" in moderate to severe asthma
- = LABA
- (= LTRA
- (= Theophylline
- (= Tiotropium
- (= Anti-IgE
- (= Anti-IL5
- (= Allergen-specific Immunotherapy
- (= Bronchial Thermoplasty

Some Patients

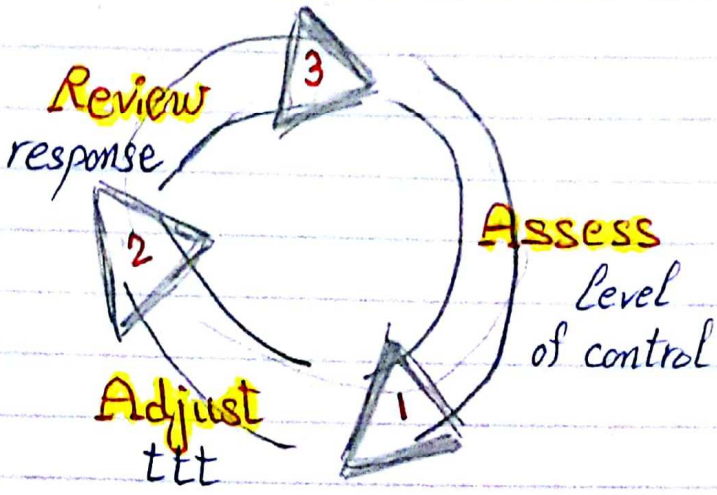
خطة العلاج
= Treatment Guidelines

فلسفتها
اختلفت تماماً
حالياً
في نقطتين جوهريتين

النقطة الأولى

* أصبحت خطة العلاج تعتمد على :
Level of control
rather than
severity of symptoms

What is called :
"Control-based Management Cycle"



النقطة الثانية

* زمان كانوا بيقولوا :
Intermittent Asthma
تاخد
reliever medication alone
without controller medication

دلوقتي أصبحوا بيقولوا :
Give
Low-dose ICS + SABA
for all asthmatic patients
even
those with intermittent symptoms
or recent-onset symptoms

‼

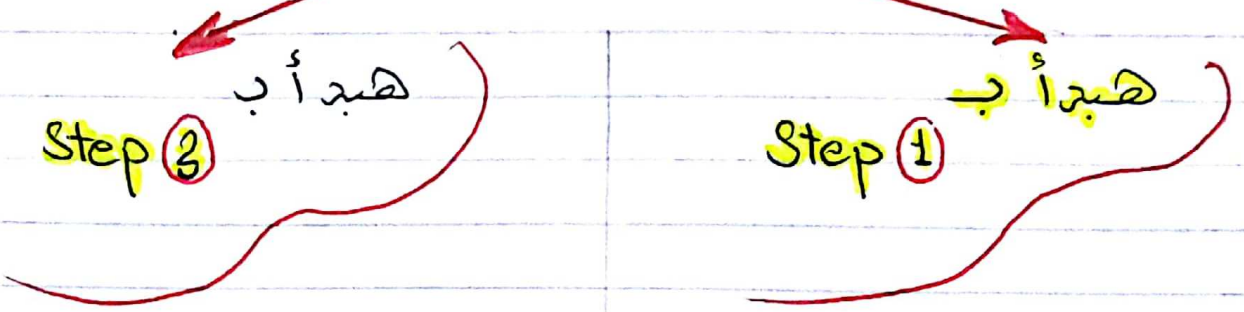
chronic airway inflammation
is found
in all patients

إذن
القاعدة الآن في العلاج

إن هبدأ لكل الحالات ب Step 2

يستثنى من هذه القاعدة

Few Cases



- If patient has "severe persistent symptoms"

- daily symptoms & need for SABA most of the days
- nocturnal symptoms & awakening ≥ 1 / week

plus

Any risk factors for exacerbation ✓

- If patient has "infrequent intermittent symptoms"

- daily symptoms & need for SABA ≤ 2 / month
- nocturnal symptoms & awakening ≤ 1 / month

plus

No risk factors for exacerbation ✓

General principles of pharmacological treatment of asthma :

" القواعد العامة للعلاج الدوائي لحالات الربو "

1. Take into account the possible reasons for uncontrolled asthma before starting or adjusting treatment for asthma ...
وهي تشمل ٨ حاجات :

1- Alternative diagnosis
2- Associated co-morbidities ---------- Allergic Rhinitis, Chronic Sinusitis, GERD, Obesity, Food Allergy
3- Lack of adherence
4- Suboptimal inhaler technique
5- Smoking (active or passive)
6- Environmental or Seasonal factors
7- Psychological factors
8- Socio-economic factors

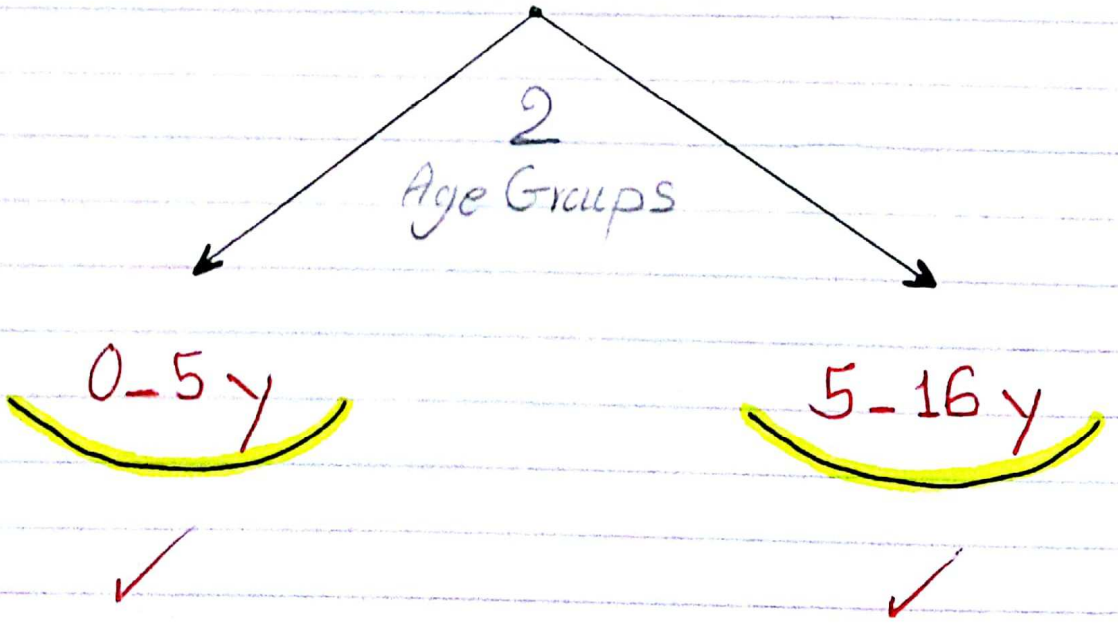
2. After starting or adjusting medications for asthma, review the response to treatment in 4-8 weeks.

3. If ICS maintenance therapy is needed, offer regular daily ICS rather than intermittent ICS therapy.
وليس عند الحاجة ✗ — تأخذ الكورتيزون تؤخذ يومياً بانتظام ✓

4. Adjust the dose of inhaled corticosteroid maintenance therapy over time, aiming for the lowest dose required for effective asthma control.

5. Ensure that a child with asthma can use his inhaler device at any asthma review.

Stepwise Approach for Treatment of Chronic Asthma in Children



طحة تاريخية
عن
(Inhalers)

وهى تعتبر واحدة من أهم الفتوحات فى الطب الحديث

يرجع الفضل فى اختراع أول (pressurized MDI) لطفلة أمريكية إسمها (سوزى)
13 y old & asthmatic child living in California
فى يوم سألت أبوها
(a very simple innocent question)
سؤال فطرى بريء لكنه عبقرى
" Why can't they put my asthma medicine in a spray , like they do for hair spray or perfume " ??

↓

Dr. George Maison ..... ? حفلها إنه أبوها كان مين
The owner of Ricker Drug Company
(صاحب شركة من أكبر شركات المستحضرات الصيدلية فى كاليفورنيا)

↓

بنته سألته السؤال ده فى ..... أبريل ١٩٥٥م
- وخلال أقل من سنة قدر يحول حلمها إلى حقيقة ؛-

↙ وظهرت للنور أول (pressurized MDI) فى ..... مارس ١٩٥٦م
وكان الدواء اللى فيها (Isoproternol)

↙ ثم بعد ١٠ سنوات تقريباً ١٩٦٨م
ظهرت بخاخة (الفنتولين)
ثم ظهرت أول بخاخة كورتيزون (Beclomethazone)

Step 1

* **Preferred option :**
  - As-needed inhaled SABA (with no controller medication)

* **Other options :**
  - Oral SABA
  - Oral short-acting theophylline

    Both are Not recommended for routine use ..... Why ?

    1- slower onset of action
    2- higher rate of side-effects

Step 2

* **Preferred option :**
  - Low-dose ICS + as-needed inhaled SABA

* **Other options :**
  - LTRA → less effective than ICS
    → may be appropriate alternative for :
    - patients unwilling to use ICS
    - patients with concomitant allergic rhinitis
  - Other options Not recommended for routine use :
    @ Cromolyn sodium
    (lower efficacy + delayed onset of action) يشتغل بعد شهر ولازم آيتا خد ٤ وقت زي البوا
    @ Sustained-release theophylline
    (lower efficacy + more side-effects)

Step 3

* **Preferred option :**
  - Low-dose ICS plus LABA + as-needed inhaled SABA

* **Other options :**
  - Medium-dose ICS
    (may be preferred option for children 5-12 y)
  - Low-dose ICS + LTRA
    (less effective)

Step 4

* **Preferred option :**
  - Medium to high dose ICS plus LABA + as-needed inhaled SABA

* **Other options :**
  - Consider adding :
    @ Tiotropium = Long-acting muscarinic antagonist (LAMA)
    (for children ≥ 6 y)
    @ Low-dose sustained release theophylline
    (less effective)
    @ Sublingual allergen immunotherapy = SLIT
    (for children ≥ 12 y)
    @ Bronchial Thermoplasty = BT
    (above 18 y)

Step 5

Refer to health care professional (Pulmonologist or Allergist)

* **Preferred option :**
  - High-dose ICS **plus** LABA **plus** third add-on therapy :
    - Long-acting muscarinic antagonist (LAMA)
      = Tiotropium (Spiriva / Respimat inhaler)
      for patients ≥ 6 y with history of exacerbations despite step 4 ttt (سعره حوالي ٥٠ دولار) ٢.٥ مكغ مرة واحدة يوميا بوريدج
    - Anti-IgE
      = Omalizumab (Xolair vial for s.c. injection)
      for patients ≥ 6 y with severe allergic asthma that is uncontrolled on step 4 ttt (سعره حوالي ٦٠٠ دولار) نوفارتس
    - Anti-IL5
      = Mepolizumab (Nucala vial for s.c. injection)
      for patients ≥ 12 y with severe esinophilic asthma that is uncontrolled on step 4 ttt (سعره حوالي ١٨٠٠ دولار) جلاكسو

* **Other options :**
  - High-dose ICS **plus** LABA **plus** low-dose oral corticosteroid (≤ 7.5 mg/day prednisolone)
  - Consider adding non-pharmacologic therapies :
    ⓐ Sublingual allergen Immunotherapy = SLIT (for patients ≥ 12 y)
    ⓐ Bronchial thermoplasty = BT (for patients ≥ 18 y)

Children < 5 y

دول Suspected Asthma (مفروض الحتة)

If persistent symptoms (or) uncontrolled with SABA alone

Consider 8-week trial with moderate dose ICS (low dose x2)

Infrequent intermittent symptoms (+) No risk factors

Offer as-needed SABA alone

If symptoms resolved, but recurred within 4 weeks of stopping ICS

If symptoms resolved, but recurred beyond 8 weeks of stopping ICS

Repeat 8-week trial of moderate dose ICS

If symptoms did not resolve

Refer to specialist to investigate for alternative diagnosis

Offer maintenance therapy with low-dose ICS + SABA

if uncontrolled in 8 weeks

Offer low-dose ICS plus LTRA + SABA

or Offer moderate-dose ICS + SABA

if uncontrolled in 8 weeks

Refer to health care professional for further investigations & management

Stepping-up asthma treatment

* **Sustained set-up :**
  - If symptoms and/or exacerbations persist despite 2-3 months of controller medication ...

بشرط

  - × symptoms are confirmed to be due to asthma
  - × inhaler technique & adherence are satisfactory
  - × modifiable risk factors have been adressed

* **Short-term set-up:**
  - for 1-2 weeks during viral infection or allergen exposure

Stepping-down asthma treatment

- Consider stepping-down ttt once good asthma control has been acheived and maintained for 3 months ... ؟ ايه الهدف من كده
  to find the lowest ttt that control both symptoms & exacerbations and minimizes side-effects.
- Choose an appropriate time for step-down (no respiratory infection or seasonal exposure).
- Stepping-down ICS doses by 25-50 % at 3 month intervals is safe for most patients.
- Don't completely withdraw ICS in adults or adolescents with diagnosis of asthma.
- Consider stopping ICS only if there have been no symptoms for 6-12 months and the patient has no risk factors.

2 Important Comments

- Where recommendations represent a change from traditional clinical practice ..... ؟ إزاي التعرف السليم
  any child whose asthma is well-controlled on his current treatment **should not** have this treatment changed just to follow the guidelines ؟

- Retrograde assessment of severity of chronic asthma can be made after treatment review :

  * If well-controlled on step (1) ⟶ Intermittent Asthma
  * If well-controlled on step (2) ⟶ Mild Persistent Asthma
  * If well-controlled on step (3) ⟶ Mod. Persistent Asthma
  * If well-controlled on step (4) ⟶ Severe Persistent Asthma
  * If uncontrolled on step (4) ⟶ Refractory Severe Asthma